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Authors

Leddy, Anna
Jaganath, Devan
Triasih, Rina
et al.

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Social Determinants of Adherence to Treatment for Tuberculosis Infection and Disease Among Children, Adolescents, and Young Adults: A Narrative Review

Anna M. Leddy,^{1,2*} Devan Jaganath,^{1,2,3*} Rina Triasih,⁴ Eric Wobudeya,⁵ Marcia C. Bellotti de Oliveira,⁶ Yana Sheremeta,⁷ Mercedes C. Becerra,⁸ and Silvia S. Chiang^{9,10,©}

¹Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, San Francisco, California, USA, ²Center for Tuberculosis, University of California, San Francisco, San Francisco, California, USA, ³Division of Pediatric Infectious Diseases, University of California, San Francisco, San Francisco, California, USA, ⁴Department of Pediatrics, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito Hospital, Yogyakarta, Indonesia, ⁵Mulago National Referral Hospital, Kampala, Uganda, ⁶Department of Pediatrics, Souza Marques Medical School, Rio de Janeiro, Brazil, ⁷All-Ukrainian Network of People Living With HIV/AIDS, Kyiv, Ukraine, ⁸Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts, USA, ⁹Department of Pediatrics, Alpert Medical School of Brown University, Providence, Rhode Island, USA, and ¹⁰Center for International Health Research, Rhode Island Hospital, Providence, Rhode Island, USA

Global efforts to eliminate tuberculosis (TB) must address the unique barriers that children (ages 0 through 9 years) and adolescents/young adults (AYA; ages 10 through 24 years) face in adhering to treatment for TB infection and disease. We conducted a narrative review to summarize current knowledge on the social determinants of treatment adherence among these age groups to guide efforts and policy to address their unique needs. Our findings revealed that research on TB treatment adherence among children and AYA is still in its nascent stage. The current literature revealed structural/community-, health system-, household-, and individual-level factors that influence treatment adherence and varied with developmental stage. There is a need to develop multilevel interventions to address the unique challenges that children and AYA face in adhering to TB treatment.

Key words. tuberculosis; medication adherence; adolescents; children; social determinants.

INTRODUCTION

Globally, an estimated 45 million children (0 through 9 years) and 217 million adolescents and young adults (AYA; 10 through 24 years) are infected with tuberculosis (TB) [1]. Of these individuals, an estimated 800 000 children and 1.8 million AYA develop TB disease each year [1, 2]. There is growing recognition that TB control programs need to focus more on children and AYA. Young children are at high risk of disease progression after TB exposure, and AYA have adult-type diseases that can contribute to ongoing community transmission [3]. At the same time, children and AYA have unique barriers to TB care [1, 4], and global efforts to eliminate TB require specific approaches that meet the needs of these populations. Adherence to treatment of TB infection, also known as TB preventive treatment (TPT), and to the treatment of TB disease remains a particular challenge for children and AYA. Studies have found that children have suboptimal adherence to treatment for TB infection and disease [5–8], and AYA with TB disease have higher rates of loss to follow-up compared to children and older adults [9–11], as well as higher TB-related mortality than

children [12]. The social determinants of TB treatment adherence in adults have been well characterized [13–15], and several large-scale interventions have been developed to address and evaluate these factors, including the use of digital adherence technologies (DATs) and conditional cash-transfer programs [16–19]. This narrative review summarizes the current knowledge on the social determinants of adherence to treatment of TB infection and disease among children and AYA, with the aim of guiding efforts to address the unique needs of these populations.

METHODS

We use the World Health Organization (WHO)'s definitions of childhood as the period before 10 years of age and adolescence/young adulthood as the period from 10 through 24 years of age. According to the WHO, adolescence spans from 10 through 19 years of age, and young adulthood, from 20 through 24 years of age [20]. We included young adults in this review because the transitions that begin in adolescence, including completion of education and establishment of an independent household, now extend into young adulthood in many different settings [21].

We searched five databases—PubMed, PsycInfo, CINAHL, Web of Science, and Google Scholar—for relevant articles using the following search terms (and variations): child, adolescent, young adult, TB, and treatment adherence. We summarized relevant studies and developed a conceptual model of the existing evidence on the social determinants of TB treatment adherence among children and AYA.

*These authors contributed equally to this work

Corresponding Author: Silvia S. Chiang, MD ScM, Center for International Health Research, Rhode Island Hospital, 55 Claverick Street, Suite 101, Providence, RI 02903, USA. E-mail: silvia_chiang@brown.edu.

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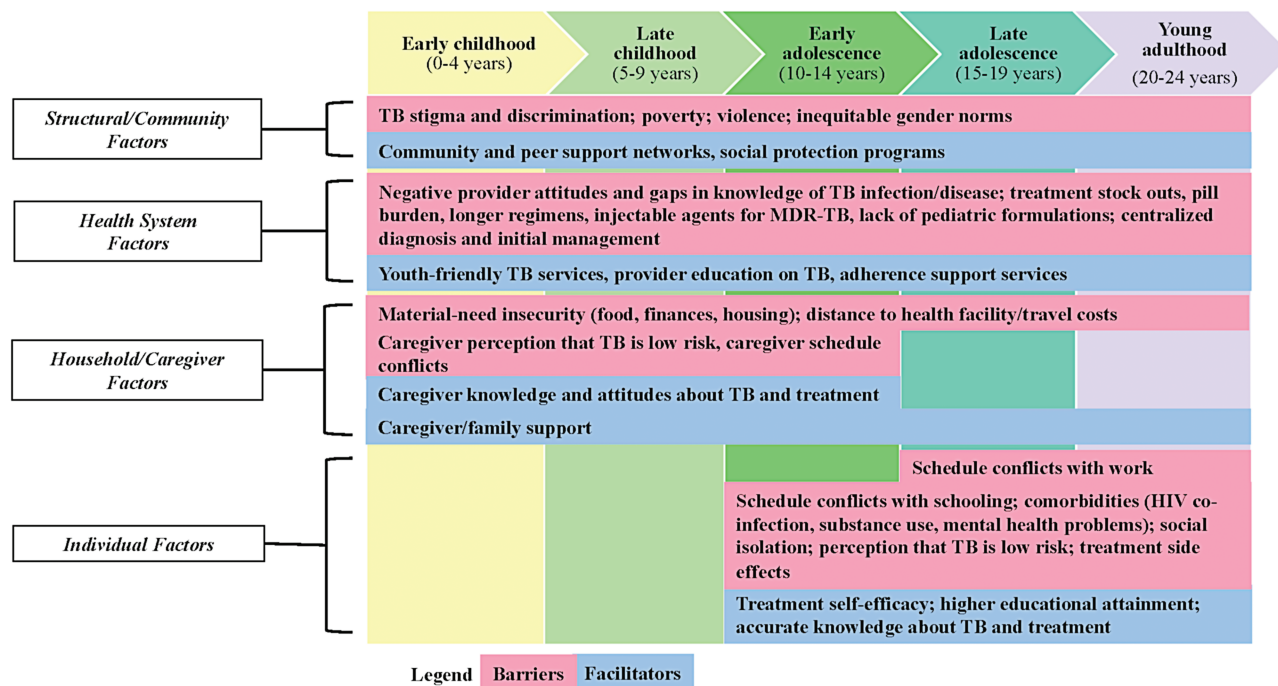


Figure 1. Barriers and facilitators to adherence to treatment for TB infection and disease among children, adolescents, and young adults, as identified in the literature. Abbreviations: HIV, human immunodeficiency virus; MDR-TB, multidrug-resistant tuberculosis; TB, tuberculosis.

RESULTS

Few studies have examined the social determinants of adherence to treatment for TB infection and disease among children and AYA. Most of the relevant research was conducted in sub-Saharan Africa, followed by South America, South and Southeast Asia, and the United States. Studies among AYA assessed adherence to treatment for both TB infection and disease, but studies among children primarily focused on adherence to treatment for TB infection. An additional limitation was that studies have traditionally defined children as those less than 15 years old and adults as those 15 years and older. This limitation prevented further stratification of factors between children and AYA and created gaps in the literature for older adolescents.

Our review revealed structural/community-, health system-, household-, and individual-level factors that influenced TB treatment adherence for infection and disease. We synthesized these findings into a conceptual model depicting the multi-level factors at different stages of childhood and adolescence/young adulthood (Figure 1). This conceptual model maps onto the socio-ecological model, which posits that individual health behaviors, such as treatment adherence, are shaped by multi-level factors [22].

Structural and Community Factors

Anticipated stigma and discrimination were found to be critical barriers to treatment adherence for TB disease and infection among children and AYA [5, 23–25], as has been previously

documented among adults [26]. In a qualitative study from Botswana, caregivers described stigma associated with frequently queuing at the TB clinic, which made it difficult for them to take their child to the clinic for daily directly observed therapy [25]. In Eswatini, adolescents with HIV had increased odds of suboptimal adherence to isoniazid preventive therapy if they believed it would lead to HIV-related stigma from their friends or neighbors [23]. AYA can also be concerned about TB-related stigma from romantic or sexual partners, with young women expressing depression and anxiety on the prospects for marriage [27–29]. Still, the association of this with adherence has not been described.

Poverty and violence are important determinants of anti-TB medication adherence. Community-level poverty shapes the resources available to patients to be able to access and receive appropriate TB care [30, 31]. Community-based violence, either as a direct effect or a reflection of underlying factors such as poverty, may also impact TB care; in Brazil, adolescents with TB living in areas with high rates of informal settlements and homicides had higher odds of unfavorable outcomes, particularly loss to follow-up [31]. Exposure to violence can be either witnessed or experienced [32], and its effect on treatment adherence needs to be further explored but is likely multifactorial. Community violence may impact adherence both directly (eg, families may be hesitant to go to the health center due to safety concerns) and indirectly (eg, violence may lead to mental health issues, which, in turn, impede adherence) [33].

Gender norms can affect TB care across the age spectrum. A study in India found that female children with multidrug-resistant (MDR)-TB did not receive equal TB care as male children and had worse outcomes [24]. Other research, primarily among people living with HIV, has demonstrated that hegemonic masculine norms, which value male toughness [34], contribute to male avoidance in seeking healthcare [35]. It is possible that such norms explain why AYA males in some settings have suboptimal TB treatment adherence compared to females [8, 36].

On the other hand, community and peer support networks may mitigate the negative effects of TB stigma and facilitate adherence to TB treatment among children and AYA [37]. Social protection programs can also promote adherence to treatment for TB disease [37, 38]; for example, in a national retrospective cohort study of AYA from Brazil, receipt of government cash transfers was associated with a reduced likelihood of an unfavorable treatment outcome [38].

Health System Factors

Provider beliefs, experience, and knowledge in the management of TB infection and disease can further influence treatment adherence [5, 39, 40]. For example, providers may believe that treatment of TB infection can increase the risk of drug resistance [41]; as a result, they may not convey the importance of treatment for TB infection to caregivers and patients. In addition, limited adherence monitoring and provider support has been linked to poor adherence among children and adolescents with TB infection and disease [5, 24, 25, 39, 42–44]. Meanwhile, studies from Kenya and Rwanda reported that strong provider counseling and support facilitated adherence to treatment for TB infection among young children [40, 43].

Treatment stock outs [25, 39, 45], pill burden [24, 43], the length of TB treatment [46, 47], and lack of pediatric formulations [41, 48] also influence adherence among children and AYA. Two large multinational trials found that shorter regimens for TB infection had significantly higher levels of adherence compared to longer regimens [46, 47]. Qualitative studies have reported the difficulty of administering TB treatment to children who cannot swallow pills. Even children who can swallow pills find it challenging to take the large number required to treat TB disease [41, 48]. Fixed-dose combinations may reduce this burden, but there is limited evidence of its role to improve adherence [49]. MDR-TB creates additional challenges for adherence [50], as its treatment involves a higher pill burden, additional adverse effects, longer duration, and the need to receive injectable agents at a clinical facility [24, 51]. The implementation of shorter all-oral MDR-TB regimens may improve adherence in children and AYA [52, 53], but this hypothesis needs to be evaluated.

The centralized model of TB care for children and young AYA also impacts adherence. In many settings, children and

young AYA (typically under age 15 years) who present to a primary care facility for TB evaluation often are referred to hospitals or other tertiary facilities because front-line providers have not been trained in the diagnosis and initial management of childhood TB [54, 55]. These referrals lead to further obstacles, including transportation costs and the need for parents to take additional time off work [41]. Moreover, without the appropriate linkage back to their primary care facility, children can be lost to follow-up [56]. Several efforts to decentralize TB management for children and AYA address these barriers to care [23, 57–59].

The lack of AYA-friendly TB services has been identified as a critical barrier to treatment adherence among this population [4, 24, 57]. Healthcare workers have reported that they lack dedicated protocols for AYA, who generally are treated the same as older adults [57]. The WHO has called for AYA-centered services, including age-appropriate TB education, adherence counseling, and support; AYA-friendly clinic spaces separated from areas for older adult patients; and alternative approaches for adherence monitoring that does not conflict with school or work hours [4].

Household/Caregiver Factors

Food, financial, and housing insecurity have been associated with poor adherence to treatment for TB infection and disease among both children and AYA [37, 38, 40, 42, 60]. Heads of households experiencing financial insecurity may prioritize getting a job instead of traveling to the clinic to collect TB medications for their children [40]. In addition, food insecurity contributes to nonadherence due to the belief that taking TB treatment without food is harmful [37, 40]. Limited money to travel to the clinic also has been cited as a barrier to accessing TB treatment and adherence among children and AYA [23, 37, 40]. These challenges may be further exacerbated when other household members have TB [61], but this link has not been evaluated in the literature.

Caregiver knowledge and attitudes about TB and its treatment play an important role in treatment adherence, particularly among younger children. For example, some caregivers have cited beliefs that children do not need treatment for TB infection since they have no symptoms of TB, while other caregivers believe that treatment for TB disease is no longer important once symptoms have resolved [5, 7, 39, 41, 45]. In contrast, children are more likely to complete treatment for TB infection if their caregivers believe in the importance of such treatment, which often occurs when another family member has had TB [5, 40, 62]. Additionally, caregivers have reported that they do not feel that they have sufficient education about TB infection or disease or training in how to give treatment to children [5, 25, 39, 63]. Education, counseling, and support to caregivers and families are facilitators that have been shown to improve treatment adherence [5, 40, 43].

Individual Patient Factors

As AYA gain more autonomy and independence, individual patient factors become more important for treatment adherence in this age group. Few studies have investigated the reasons why AYA have lower adherence to TB treatment as compared to younger children or older adults [11, 38, 44, 64]. The growing need for autonomy, reduced reliance on caregivers, greater dependence on peers and romantic/sexual partners, and increased focus on short-term gains over long-term health outcomes may all play a role, but these factors have not been evaluated in AYA with TB [1, 60, 65, 66]. Educational attainment among AYA TB patients and their caregivers impact adherence to treatment for TB infection and disease [23, 38, 42]. AYA knowledge and attitudes about TB and its treatment likely influence adherence, as has been observed in adults [26], but we were unable to find specific studies in AYA that assessed this association.

Self-efficacy, which refers to individuals' belief in their own ability to carry out a specific behavior [67, 68], predicts adherence to HIV treatment in AYA [69]. However, limited research has explored the role of self-efficacy in TB treatment adherence. We found one study that demonstrated that self-efficacy for collecting TB medicines monthly was associated with reduced odds of suboptimal treatment adherence among adolescents and caregivers of children with TB infection [23].

Co-morbidities, specifically TB-HIV coinfection [31, 36, 38, 70] and substance use [31, 38], have been associated with poor treatment adherence for TB disease among AYA. TB disease is additionally associated with poor mental health, particularly among AYA, due to prolonged home isolation or hospitalization for infection control purposes, and experienced and/or internalized stigma [23, 24, 37, 66]. In one study from India, adolescent TB patients described feelings of loneliness, anger, and anxiety because they missed school and playing with their friends [24]. More so than children, AYA living with TB disease internalize TB stigma, which likely leads to poor mental health outcomes and suboptimal treatment adherence [37].

DISCUSSION

Our findings indicate several gaps in the literature (Table 1) and the need to develop multi-level interventions to address the unique challenges that children and AYA face in adhering to TB treatment. At the structural level, interventions need to address TB stigma and inequitable gender norms for children and AYA, and foster community and peer support networks for adherence. Social protection programs can further address household material-need insecurities, such as cash transfers and food support [71, 72]. At the health-systems level, greater understanding of child and AYA preferences is needed to develop age-appropriate TB services. These services include greater decentralization and improved linkage to care to primary care facilities to reduce loss to follow-up [56]. Our findings also suggest the need to ensure

Table 1. Research Gaps on the Social Determinants of TB Treatment Adherence in Children and Adolescents and Young Adults

Structural/Community Factors
<ul style="list-style-type: none">• Pathways of how exposure to violence creates barriers to adherence• Interventions to address TB-related stigma and inequitable gender norms for children and AYA• Role of social protection programs and peer support networks for children and AYA with TB
Health System Factors
<ul style="list-style-type: none">• Child and AYA needs and preferences to develop age-appropriate services• Impact of fixed-dose combinations and all-oral MDR TB regimens on adherence• Influence of novel adherence monitoring tools, including digital adherence technologies, on adherence• Effect of decentralized TB care on adherence
Household/Caregiver Factors
<ul style="list-style-type: none">• Influence of TB illness in additional household members, including the caregiver of the child/AYA, on adherence• Interventions to address household material-need insecurities to improve adherence
Individual Factors
<ul style="list-style-type: none">• Influence on adherence of caregiver and patient knowledge and attitudes about TB disease and treatment• Effect of developmental changes during adolescence and young adulthood on adherence, including a shifting emphasis from family relationships to peer relationships• Role of self-efficacy to support TB treatment adherence• Interventions to support mental health during TB treatment
Other Research Needs
<ul style="list-style-type: none">• Wider geographic representation• Additional studies on adherence to TB disease treatment in children• Greater inclusion of older adolescents

Abbreviations: AYA, adolescents and young adults; MDR, multidrug-resistant; TB, tuberculosis.

providers are trained to educate caregivers, children, and AYA about TB infection and disease. Better adherence monitoring and support systems need to be developed; for example, DATs—including mobile phone short messaging service texts or calls, digital pill boxes, and video-based observed therapy [73]—may be a particularly promising option given the high level of technology and mobile phone use in youth around the world [74, 75]. At the same time, these technologies need to be adapted to the unique developmental stages of children and AYA [76]. At the individual level, better integration of TB care with other child and AYA health services is needed, including for HIV, substance use, and mental health [23, 24, 37, 66, 77]. Peer support groups and peer treatment navigators have supported mental health and HIV treatment adherence, and may also be helpful for TB [78, 79]. The goal of this multilevel approach would be to provide caregivers, children, and AYA with the knowledge, resources, support, and self-efficacy to complete treatment for TB infection and disease.

CONCLUSION

Research on the social determinants of TB treatment adherence among children and AYA is still in its nascent stage. However, the current literature suggests the need for multi-level,

developmentally-sensitive interventions to address the unique barriers to TB treatment adherence for children and AYA. Such interventions should be incorporated into global TB elimination strategies.

Supplementary Data

Supplementary materials are available at *Journal of the Pediatric Infectious Diseases Society* online (<http://jpid.oxfordjournals.org>).

Notes

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